REMARKS

Reconsideration of the above-identified application in view of the amendment above the remarks below is respectfully requested.

No claims have been canceled in this paper. Claims 1, 14 and 15 have been amended in this paper. New claims 43-44 have been added in this paper. Therefore, claims 1-31 and 35-44 are pending. Of these claims, claims 35-42 have been withdrawn "as being drawn to non-elected Groups." Therefore, claims 1-31 and 43-44 are under active consideration.

Claims 1-31 stand rejected under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention." In support of the rejection, the Patent Office states the following:

> Claim 1 recites the limitation "said individual, tissue, cell, or other biological material containing DNA" in lines 9-10. There is insufficient antecedent basis for this limitation in the claim as it is unclear if it is referring to the "individual, tissue, cell, or other biological material containing DNA" from step (a) or (b) which are not necessarily the same. Clarification of this issue via clearer claim wording is requested. Claims 2-31 are also rejected due to their dependency from claim 1.
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> Claim 1 recites the limitation "said individual" in lines 5-6 and 9-10. There is insufficient antecedent basis for this limitation in the claim. Lines 4 and 8 recite "at least one individual" which means that there can be more than one individual. In this scenario of multiple individuals, it is unclear which individual is being referred to in the "said individual" limitation. It is also unclear if the phrase "at least one individual" in steps (a) and (b) are referring to the same at least one individual. Clarification of this issue may be rectified by amending the limitation to "said at least one individual." Clarification of this issue via clearer claim wording is requested. Claims 2-31 are also rejected due to their dependency from claim 1.

> Claims 14 (line 3) and 15 (line 3) recite the phrase "associated with" which is vague and indefinite. It is unclear what parameters and to what degree these parameters must be met to be considered "associated with." Clarification of the metes and bounds of the claims via clearer claim wording is required.
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> Claims 17 (line 2) and 25 (line 2) recite the phrase "dependent upon" which is vague and indefinite. It is unclear what parameters and to what degree these parameters must be met to be considered "dependent upon". Clarification of the metes and bounds of the claims via clearer claim wording is required.
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> Applicants state that the claims have been revised and are now definite. The newly amended phrases mentioned above are indefinite for the reasons given above.

Applicants respectfully traverse the subject rejection. Insofar as the subject rejection relates to claim 1, Applicants note that claim 1 has been amended so that the language in question is no longer recited. Insofar as the subject rejection pertains to claims 14 and 15, Applicants respectfully disagree with the Patent Office's position that "associated with" is indefinite. Nevertheless, in an effort to place the application in condition for allowance, Applicants have replaced "associated with" with "operatively linked to." Applicants respectfully submit that one of ordinary skill in the art, having read the present specification, would understand what is meant by this language. Insofar as the subject rejection pertains to claims 17 and 25, Applicants respectfully traverse. The mere fact that the language in question is broad does not render it indefinite. Applicants respectfully submit that one of ordinary skill in the art, having read the present specification, would understand what is meant by the language in question.

Accordingly for at least the above reasons, the subject rejection should be withdrawn.

Claims 1-11, 13-21, 23-26, 28 and 31 stand rejected under 35 U.S.C. 102(e)(2) "as being anticipated by Laird et al. (P/N 6,311,393 B1)." In support of the rejection, the Patent Office restates the reasons from its January 12, 2005 Office Action and then states the following:

> Applicants reiterate the rejection as well as amended claim 1. Applicants argue that Laird et al. do not disclose a method comprising the steps of obtaining a biological sample A [that] was exposed to at least one drug, chemical substance and/or pharmaceutical composition; obtaining sample B that was not exposed to at least one drug, chemical substance and/or pharmaceutical composition; and then analyzing the level of cytosine methylation at chosen sites of the DNA contained in the samples A and B. This statement is found unpersuasive as Laird et al. disclose treating genomic DNA with sodium bisulfite and comparing it to a control (see above 35 USC 102 rejection). It is further noted that instant claim 1 does not state that biological sample A was exposed and biological sample B was [not] exposed, but rather the individual, tissue, cell or other biological material containing said DNA was either exposed or not exposed.
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> Applicants argue that sodium bisulfite does not constitute the claimed drug, chemical substance and/or pharmaceutical composition. This statement is found unpersuasive as sodium bisulfite is a chemical substance. Furthermore, Applicants did not provide any clear and complete definition of "chemical substance" in the originally filed disclosure that would exclude sodium bisulfite.
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> Applicants again submit that claim 1 requires biological sample A be exposed to the claimed drug, that the biological sample B not be exposed to the claimed drug and that the level of cytosine methylation in samples A and B be analyzed. Again, it is noted that instant claim 1 does not state that biological sample A was exposed and biological sample B was [not] exposed, but rather the individual, tissue, cell or other biological material containing said DNA was either exposed or not exposed. It is further noted that the claims state that exposure or non-exposure can be to a drug, chemical substance and/or pharmaceutical composition, not necessarily only a drug. Applicants argue that Laird et al. do not disclose exposing Sample A to sodium bisulfite and not exposing Sample B to sodium bisulfite and then analyzing cytosine methylation after exposure or non-

> exposure to sodium bisulfite. This is found unpersuasive as instant claim 1 does not state that the steps must be performed in a particular order (i.e. before and after), but rather that the method comprises the steps.
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> Applicants argue that the specification notes that one of the principal purposes of the present invention is to provide a method for determining the effect of a drug, chemical substance and/or pharmaceutical composition on the methylation pattern of DNA. It is noted that limitations from the specification cannot be read into the claims unless that limitation is specifically recited in the claims. Applicants argue that Laird et al. teach sodium bisulfite treatment has no effect as it does not alter the methylation state of DNA. Applicants did not point to where this passage is found, but it is noted that instant claim 1 recites concluding "the biological effect and/or activity". It is noted that the claims do not recite whether the effect is direct or indirect. It is noted that having no effect is a possible conclusion about biological effect and/or activity while performing a scientific experiment. In addition, methylation amounts quantify an "activity". Applicants have recited terms, such as "biological effect" and "activity" in instant claim 1 which have been broadly and reasonably interpreted. Applicants argue that Laird et al. do not disclose step (b). This statement is found unpersuasive as a control reaction (col. 5, lines 61-64) represents an unexposed sample. Applicants' arguments are deemed unpersuasive, such that the 35 USC 102 rejection is maintained.

Applicants respectfully traverse the subject rejection. Claim 1 has been amended herein and now recites "[a] method for determining the biological effect and/or activity of at least one drug, chemical substance and/or pharmaceutical composition, comprising the steps of:

(a) obtaining a biological sample A containing DNA, said biological sample A being from at least one of an individual, a tissue, a cell or another biological material containing DNA, wherein said biological sample A was exposed to said at least one drug, chemical substance and/or pharmaceutical composition;

(b) obtaining a biological sample B containing DNA, said biological sample B being from at

least one of an individual, a tissue, a cell or another biological material containing DNA, wherein said biological sample B was not exposed to said at least one drug, chemical substance and/or pharmaceutical composition;

(c) then, analyzing the level of cytosine methylation at chosen sites of the DNA contained in the biological samples A and B;

(d) selecting the sites which are differentially methylated between the DNA in biological samples A and B, whereby a knowledge base is generated; and

(e) concluding from the said knowledge base on the biological effect and/or activity of said at least one drug, chemical substance and/or pharmaceutical composition of said biological sample A from step (a)."

Thus amended, claim 1 now explicitly requires, among other things, (i) that biological sample A be exposed to the drug, chemical substance and/or pharmaceutical composition, (ii) that biological sample B not be exposed to the drug, chemical substance and/or pharmaceutical composition, and (iii) that, after said exposure or non-exposure, the level of cytosine methylation in biological samples A and B be analyzed. Therefore, to the extent that the Patent Office's rejection is predicated on the position that "instant claim 1 does not state that the biological sample A was exposed and biological sample B was [not] exposed, but rather the individual, tissue, cell or other biological material containing said DNA was either or not exposed," the Patent Office's position is not supported by the present language of claim 1, which refers to the exposure or non-exposure of biological samples A and B.

Similarly, to the extent that the Patent Office's position is predicated on the position that

"instant claim 1 does not state that the steps [, i.e., exposure or non-exposure to the drug, chemical substance and/or pharmaceutical composition, followed by analyzing cytosine methylation,] must be performed in a particular order (i.e. before and after), but rather that the method comprises the steps," Applicants respectfully submit that the Patent Office's position is not supported by the present language of claim 1, which requires that the analysis take place after either exposure or non-exposure.

In view of the above, claim 1 is patentable over Laird et al. for the reasons detailed in the Amendment of June13, 2005, which paper is incorporated herein by reference.

Accordingly, for at least the above reasons, the subject rejection should be withdrawn.

Applicants note that claims 12, 22, 27 and 29-30 have not been rejected on the basis of any prior art, but rather, have been rejected solely on the basis of their dependence from claim 1, claim 1 having been rejected under 35 U.S.C. 112, second paragraph. Therefore, in view of the fact that Applicants have overcome said rejection of claim 1 under 35 U.S.C. 112, second paragraph, the immediate allowance of claims 12, 22, 27 and 29-30 is respectfully requested.

New claims 43 and 44 have been added in this paper. No new matter is added thereby, and claims 43 and 44 are readable on the elected species. Claims 43 and 44 are patentable over Laird et al. for at least the reason that Laird et al. does not teach or suggest "[a] method for determining the biological effect and/or activity of at least one drug, chemical substance and/or pharmaceutical composition, comprising the steps of:

(a) obtaining a biological sample A containing DNA, said biological sample A being from at least one of an individual, a tissue, a cell or another biological material containing DNA, wherein

said biological sample A was exposed to said at least one drug, chemical substance and/or pharmaceutical composition;

(b) obtaining a biological sample B containing DNA, said biological sample B being from at least one of an individual, a tissue, a cell or another biological material containing DNA, wherein said biological sample B was not exposed to said at least one drug, chemical substance and/or pharmaceutical composition;

(c) then, analyzing the level of cytosine methylation at chosen sites of the DNA contained in the biological samples A and B, wherein said analyzing comprises chemical treatment with at least one of bisulfite, hydrogen sulfite or disulfite;

(d) selecting the sites which are differentially methylated between the DNA in biological samples A and B, whereby a knowledge base is generated; and

(e) concluding from the said knowledge base on the biological effect and/or activity of said at least one drug, chemical substance and/or pharmaceutical composition of said biological sample A from step (a)."

In particular, Laird et al. does not teach or suggest obtaining a biological sample A that was exposed to at least one drug, chemical substance and/or pharmaceutical composition; obtaining a biological sample B that was not exposed to at least one drug, chemical substance and/or pharmaceutical composition; and then analyzing analyzing the level of cytosine methylation at chosen sites of the DNA contained in the biological samples A and B, wherein said analyzing comprises chemically treating each of biological samples A and B with at least one of bisulfite, hydrogen sulfite or disulfite.

In conclusion, it is respectfully submitted that the present application is now in condition for allowance. Prompt and favorable action is earnestly solicited.

If there are any fees due in connection with the filing of this paper that are not accounted for, the Examiner is authorized to charge the fees to our Deposit Account No. 11-1755. If a fee is required for an extension of time under 37 C.F.R. 1.136 that is not accounted for already, such an extension of time is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on February 14, 2006

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